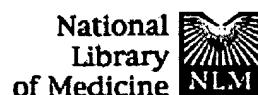


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Role of glycosyl-phosphatidylinositol hydrolysis as a mitogenic signal for epidermal growth factor.

Clemente R, Jones DR, Ochoa P, Romero G, Mato JM, Varela-Nieto I.

Instituto de Investigaciones Biomedicas, Consejo Superior de Investigacione Cientificas (CSIC), Madrid, Spain.

We have investigated the role of the hydrolysis of glycosyl-phosphatidylinos (GPI) as one of the signalling pathways elicited after interaction of epiderma growth factor (EGF) with its specific plasma membrane receptor (EGFR). Endogenous GPI was characterized in both NIH 3T3 mouse fibroblast cells a in EGFR-transfected NIH 3T3 cells (designated EGFR T17). GPI molecules isolated from both cell lines were identical and they incorporated radioactivit from both sugar and fatty acid substrates. Incubation of EGFR T17 cells with EGF, produced a rapid and transient hydrolysis of GPI. Maximum hydrolysis occurred after a 1-min incubation with 50 nM EGF. No such effects of EGF were observed in the parental cell line. Both inositol phosphoglycan (IPG)- a EGF-induced cell proliferation was inhibited in the presence of an IPG-antib to different extents. The relationship between GPI hydrolysis and the activity the EGFR was studied using the tyrosine kinase inhibitors tyrphostin (RG50864) and genistein. These agents were able to significantly inhibit EG mediated cell proliferation, EGF-dependent hydrolysis of GPI and EGF-regulated autophosphorylation of the EGFR. It is concluded that GPI hydroly is one of the earliest intracellular events generated in response to EGF.

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